REMARKS

Claims 1-7 are pending in this application. Claims 1 and 7 are hereby amended. Applicants maintain that the instant amendments to claims 1 and 7 address all of the outstanding grounds for rejection imposed in the July 14, 2003 Office Action issued in the instant application and that each of the pending claims 1-7 are in a condition for allowance.

Applicants have submitted a corrected version of Figure 15 with this Amendment. There has been no change in the amino acid sequence of Figure 15 or its substantive description. Rather, Figure 15 has been corrected to show the amino acid sequence of the epitope for the anti-α1-I domain blocking mAbs (Val-Gln-Arg-Gly-Gly-Arg (SEQ ID NO:8)) in the box depicted in the figure. Corrected Figure 15 therefore conforms to the specification amendments entered in the Response to February 11, 2003 Office Action submitted in the instant application.

35 U.S.C. § 112, ¶ 2.

Claims 1-7 as pending in the instant application were rejected as indefinite under 35 U.S.C. § 112, ¶ 2, for failing to particularly point out and distinctly claim the claimed invention. Applicants maintain that the proposed amendments to claim 1 obviate the alleged basis for this rejection and that the amended claim particularly points out and distinctly claims a method for the treatment of arthritis comprising administering to a subject suffering from arthritis a composition comprising a function blocking antibody or a fragment of said antibody capable of binding an epitope of VLA-1, wherein the epitope comprises the amino acids Val-Gln-Arg-Gly-Gly-Arg (SEQ ID NO:8) or equivalents thereof, or naturally occurring variants thereto, and wherein the amount of function blocking antibody or a fragment of the antibody in the composition administered to the subject is effective to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject.

It is clear from the proposed amendment to claim 1, and claims 2-7 that depend from claim 1, that the epitope comprises the amino acids Val-Gln-Arg-Gly-Gly-Arg (SEQ ID NO:8) or equivalents thereof, or naturally occurring variants thereto.

35 U.S.C. § 102(e).

Claims 1-6 were rejected under 35 U.S.C. § 102(e)("Section 102(e)") as being anticipated by U. S. Patent No. 5,788,966 ("*Chess*"). The Examiner asserted that function blocking is inherent in *Chess* and maintained that the burden was on Applicants to show that *Chess* does not inherently disclose use of a mAb capable of binding an epitope of VLA-1, wherein the epitope comprises the amino acids Val-Gln-Arg-Gly-Gly-Arg (SEQ ID NO:8) and wherein the mAb is administered in an amount effective to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject. The Examiner maintained that the Applicants did not provide objective evidence refuting such an inherent disclosure. Applicants respectfully submit that this rejection was improper for the following reasons.

Initially, Applicants wish to clarify that it is not their position that the *Chess* mAb does not target the same epitope as that targeted in the pending amended claims. Rather, it is Applicants' position that even if the *Chess* mAb does target the same epitope -which it may-the Applicants' claimed methods of treatment are not expressly or inherently anticipated by *Chess* for the following reasons.

Chess notes that the synovial fluid of arthritis patients expresses enhanced levels of VLA-1, discloses that mAb 1B3.1 affects the interaction of VLA-1 and T cells in conditions where enhanced levels of VLA-1 are noted, and observes that the synovial fluid of arthritis patients expresses enhanced levels of VLA-1 (*see* Response to February 11, 2003 Office Action). However, *Chess* does not expressly or inherently anticipate any of the claims because there are manipulative differences between the steps of each of the pending claims and the disclosure of Chess. *See Bristol Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 58 U.S.P.Q. 2d 1508 (Fed. Cir. 2001).

Chess does not disclose, either expressly or inherently, administration of an antibody or antibody fragment in a dosage of between about 10 mg to about 250 mg administered over a dosing period of between about one to about seven days to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject. *Chess* therefore does not expressly or inherently anticipate any of the

pending claims, irrespective of whether Applicants' and *Chess's* mAb's target the same epitope.

Applicants'claims use a specific dosage regimen in order to achieve a specific therapeutic endpoint; neither this dosage regimen or associated therapeutic endpoint is disclosed in *Chess*. Applicants' claimed inventions do not merely constitute an appreciation of a previously unknown aspect of an otherwise known process; the dosages and therapeutic endpoints recited in the claimed methods differentiate the claims from *Chess*. *Rapoport v. Dement, et al.*, 59 U.S.P.Q. 2d 1215 (Fed. Cir. 2001) (claimed method of treating sleep apnea by administration of an azapirone not anticipated by known anti-anxiety use of buspirone, even though anxiety was associated with sleep apnea and prior art disclosed use of the same total daily dosages). Whether or not viewed as claims to patentably distinct species within a generic disclosure of *Chess*, Applicants' claims, as amended, are patentably distinct over *Chess*. *See Rapoport.*

35 U.S.C. § 103(c).

Applicants confirm that the subject matter of all of the pending claims was commonly owned at the time the inventions claimed therein were made.

The Examiner has maintained that there was a sufficient motivation, based on the level of ordinary skill in the art alone, to combine: *Chess's* disclosure that monoclonal antibody 1B3.1 binds to a distinct VLA-1 epitope; *Riikonen's* disclosure that the mAb SR-84 blocks the function of α1β1 integrin and that in HeLa cells α1β1 integrin acts as a receptor for certain types of collagen; and *Fabbri's* disclosure that the FB12 mAb is functional in that it blocks the adhesion of activated T lymphocytes to fibronectin, collagen type IV and laminin, to yield the inventions of claims 1-7. According to the Examiner, *Fabri* "provide[s] a clear direction, motivation and expectation of success in treating arthritis with α1β1-specific antibodies." In fact, neither *Fabri* nor the level of ordinary skill in the art provided any motivation to cobble together the cited references in the manner suggested to yield the claimed inventions.

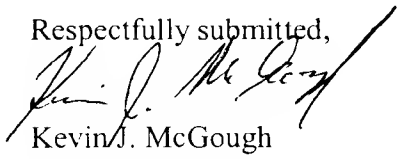
Fabbri's disclosed that the FB12 mAb binds to ECM, which, according to *Riikonen*, is found in the synovial lymphocytes of patients with rheumatoid arthritis. *Fabbri* concluded that the FB12 mAb "may represent a useful reagent for the study of the

biological function of α1-1 integrin I domain" and also stated that the disclosed results "suggest that the α1-1 domain has a functional role in lymphocyte binding to ECM proteins, including FN." *Fabbri, p. 50.* This was not a clear motivation to combine the cited references to yield the specific methods of treatment recited in the pending and new claims. It can be construed as a conjecture that maybe the FB12 mAb could serve as a research tool to learn more about the α1-1 domain.

Chess, *Fabri*, and *Riikonen*, whether taken alone or in any combination, do not suggest the therapeutic endpoint and dosage regimen recited as limitations of the pending amended claims and do not render any of the claims obvious. There is no basis to conclude that those of ordinary skill in the art would have understood *Fabri* as somehow clarifying that either *Chess* or *Riikonen* suggested treating arthritis or rheumatoid arthritis by using the dosage regimens specified in the pending claims to achieve the specified therapeutic endpoint of such claims. The references, whether taken alone or in any combination, simply do not disclose that such particular dosage regimens would achieve the defined therapeutic endpoint. *Cf. In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Given the foregoing, the combination of *Fabri*, *Chess*, and *Riikonen* suggested by the Examiner in the July 14, 2003 Office Action was premised on impermissible hindsight.

In light of all of the foregoing, it is respectfully maintained that the instant amendments and remarks address all of the grounds for rejection raised by the Examiner. Accordingly, Applicants respectfully maintain that all of the pending claims should be passed to issue.

Respectfully submitted,



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